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Predictors of quality of life 1 year after minor stroke or TIA: a prospective single-centre cohort study

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ABSTRACT

Objectives In patients after a transient ischaemic attack (TIA) or minor stroke, dysfunction is often underestimated by clinical measures due to invisible symptoms, including cognitive and emotional problems. Many of these patients need stroke care programme, but others do not. In this study, we aim to identify potential predictors of quality of life (QoL) in patients with TIA or minor stroke 1 year poststroke to be able to select which of these patients will need aftercare.

Design Prospective observational cohort study.

Setting Single-centre hospital in the Netherlands.

Participants 120 patients, diagnosed with TIA or minor stroke and discharged without rehabilitation treatment, completed the study.

Primary and secondary outcome measures QoL (RAND-36), anxiety and depressive symptoms (Hospital Anxiety and Depression scale), the degree of disability or functional dependence after stroke (modified Rankin Scale (mRS)) and symptoms of anxiety and depression specific to stroke (SSADQ) were assessed at baseline (2–6 weeks poststroke) and compared with follow-up at 1 year poststroke.

Results Depression (B=−1.35, p<0.001) and anxiety (B=−0.57, p=0.041) at baseline predicted a worse mental component of QoL after 1 year. Depression (B=−1.100, p<0.001) at baseline, but also age (B=−0.261, p=0.002) and female sex (B=4.101, p=0.034) predicted a worse physical component of QoL after 1 year.

Conclusion With the identification of these predictors, we might be able to select more efficiently and timely the patients with TIA or minor stroke who need stroke aftercare.

Strengths and limitations of this study

- In this prospective study, potential predictors of quality of life were included after thorough consideration based on previous research.
- The sample size of the study was calculated based on the number of predictors.
- A considerable part of our study population of patients who suffered a transient ischaemic attack or minor stroke was excluded due to several reasons, but no differences were found in patient characteristics between the study population and the excluded patients.
- During follow-up, there was no insight into outpatient rehabilitation care, changes in medication or employment.

INTRODUCTION

Although mortality rates have declined, the incidence of ischaemic stroke has remained stable or even increased slightly.[1] As a consequence of stroke, many patients experience persistent deficits and reduced functional independence.[2] According to a recent report from the Global Burden of Disease (GBD) 2016 Lifetime Risk of Stroke Collaborators, cerebrovascular disease ranks second in leading causes of disability-adjusted life years globally, with the burden of disease increasing proportionally to age and in the more developed regions.[3] Based on severity and duration, ischaemic stroke can be classified as major and minor stroke and transient ischaemic attack (TIA).[4 5]

Patients with major stroke and severe debilitating symptoms usually receive further rehabilitation treatment.[2] In contrast, full recovery is assumed in patients with minor stroke or TIA, and these 'walking and talking' patients are discharged home from the hospital without rehabilitation.[6] However, previous studies found that a substantial proportion of these patients do suffer from invisible symptoms, including cognitive and emotional problems.[6–13] When assessment only includes clinical measures such as the modified Rankin Scale (mRS), these problems can easily be overlooked. Nevertheless, these complaints can be a major contributor to poor quality of life (QoL).[6–8] In the past few years, this problem has been addressed by the introduction of many outpatient stroke care programmes targeting patients with minor stroke or TIA. Evidence is accumulating that these outpatient stroke care programmes may improve QoL and self-efficacy 3–12 months poststroke.[14 15] However, a significant group of patients without residual signs or symptoms do not need this aftercare. The scarce resources and time of healthcare professionals

in stroke could, therefore, be spend more efficiently by only giving the stroke care programme to patients who really need this. In terms of costs, it would be efficient to be able to select which patients might need care and who do not. Little is known about which factors might predict invisible symptoms after 1 year. This study aims to identify potential predictors associated with a lower QoL 1 year after the stroke to be able to select which 'walking and talking' patients will need aftercare.

METHODS

Study design

From January 2016 to May 2018 at OLVG Oost hospital, medical records of patients admitted with TIA or minor stroke 1 year ago were screened for participation in this prospective cohort study. TIA and minor stroke were defined as acute neurological deficits that fully resolve within 24 hours and 3 days, respectively, followed by discharge from the hospital without the need for rehabilitation treatment. These patients had a mRS of <2 (see the Health outcomes section). As part of standard clinical care, patients with TIA and stroke discharged to home are re-evaluated by a specialised stroke nurse shortly after discharge. All patients with residual or new symptoms are referred to the Beroerte Adviescentrum (BAC), a Stroke Advice Centre in Amsterdam for further outpatient care where health outcomes are assessed at baseline (i.e., shortly after the TIA or stroke). The BAC is a service in Amsterdam run by nurses to support patients discharged home after stroke to improve independence and self-rehabilitation. Because patients can only participate in this study when baseline assessments were completed, patients who were not referred to BAC or did not complete baseline assessments were excluded. Furthermore, patients were excluded if below 18 years of age, if insufficiently proficient in Dutch or if they had dementia or behavioural disorders compromising study participation. The study received full ethical approval and all included patients gave written consent.

Participants

Eligible patients were initially contacted by telephone. Following verbal consent, paper study materials were sent by mail and included study information, consent form, forms for assessing health status at 1 year poststroke and a form for obtaining sociodemographic information. After written consent and the completed study forms were returned, a telephone-based assessment of the mRS was done. Additional clinical data were collected from medical records. Baseline health status was assessed 1 year prior as part of standard clinical care (figure 1).

Patient and public involvement

The aim and objective of this study have been based on the need for better patient-tailored aftercare for patients with TIA or minor stroke. As experiences of patients who had a TIA or minor stroke and previous research in stroke care revealed unrecognised symptoms and burden of disease, earlier and improved identification of patients 'at risk' could be beneficial for the long-term QoL after stroke. However, we did not involve patients or patient advisers in the design, recruitment or conduct of the study. In our study, all health outcomes were completed on paper surveys at home, and structured telephone interviews. Participants were easily accessible by telephone allowing better recruitment and participation rates. The results of this study will be disseminated to all study participants by letter at the end of the study, as stated in the informed consent form.

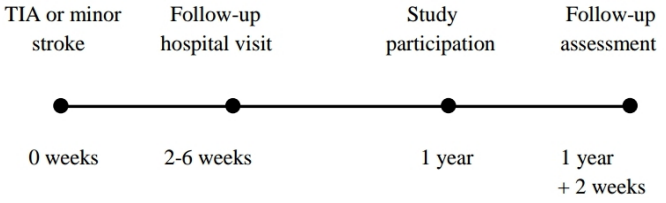

Figure 1 Flowchart of the study.

Health outcomes

Health outcomes were assessed at baseline as part of standard clinical practice and 1 year poststroke (follow-up) as part of this study. QoL was assessed with the research and development-36 scale (RAND-36), one of the most widely used health-related quality of life (HRQoL) survey instruments in stroke.[16 17] It comprises 36 items, assessing the following health domains: physical functioning, social functioning, role limitations due to physical problems, role limitations due to mental problems, mental health, vitality, bodily pain, fatigue, general health and health change. These domains can be scored into scale scores, from which two summary scores can be derived: a physical (PCS) and a mental (MCS) component score. The scores range from 0 to 100, with higher scores reflecting better outcome. The RAND-36 has been translated and validated into multiple languages, including Dutch. The minimal clinically important difference (MCID) for the RAND-36 is in the range of 3–5 points.[17] In this study, the Dutch RAND-36 V.2 was used.

Depression and anxiety were assessed with the Hospital Anxiety and Depression Scale (HADS), an extensively researched and validated scale for the measurement of anxiety and depression.[18] The HADS consists of 14 questions graded on a 4-point rating scale. Subsequently two subscales, anxiety (seven items) and depression (seven items), can be calculated by summing their respective items. A score between 7 and 10 suggests probable anxiety or depressive disorder, whereas a score of 11 or higher is indicative of an anxiety or depressive disorder. The MCID for the HADS in patients with cardiovascular disease is 1.7 points.[19] In addition, the Stroke-Specific Anxiety and Depression Questionnaire (SSADQ), developed by neuropsychologists for the assessment of symptoms of anxiety and depression specific to stroke, was assessed. This questionnaire, although not validated, was thought to be more sensitive than the HADS in this stroke population.

The degree of disability or functional dependence after stroke was assessed with the mRS, an outcome measurement scale ranging from 0 (no limitations or symptoms in activities of daily living) to 5 (bedridden) and 6 (death). The mRS is also shown to be reliably assessed through telephone interviews.[20] Baseline mRS was assessed in person by one of three stroke nurses of the BAC at 3 months postevent. Follow-up mRS was assessed through a semi-structured telephone interview by one of four researchers, who all completed an online video-based training developed by Quinn *et al*.[21 22] Sociodemographic characteristics collected at follow-up were: marital status (married, unmarried or widowed); level of education, assessed on a Dutch 7-point scale (Schaal van Verhage) and afterwards stratified into three groups: low (1-2), average (3-5), high (6-7); current living arrangement (alone or with spouse/relative(s)); recurrence of TIA, ischaemic or haemorrhagic stroke during the period between onset of stroke and follow-up.

Statistical analysis

Mean, median and the visual inspection of histograms and P-P plots were used to assess whether or not the data were normally distributed. Independent samples *t*-test and χ^2 test were used for assessing differences in patient characteristics. Changes between baseline and follow-up health outcomes were assessed using paired samples *t*-tests and Wilcoxon signed-rank tests for data distributed normally and non-normally, respectively. Multiple linear regression analysis was performed for the identification of predictors of QoL, using a stepwise backward elimination method with a p-value of >0.10 set as the threshold for elimination.[23] For the remaining analyses, a p-value of <0.05 was considered to be statistically significant. The following 12 predictors were entered at the beginning of the analysis: marital status, HADS depression score, HADS anxiety score, SSADQ score, recurrence of TIA or minor stroke, living arrangement, level of education, age, sex, mRS score, incidence, location of TIA or minor stroke. These predictors have been carefully selected based on previous research.[24–29] Given that marital status and degree of education were categorical variables, dummy variables were used in this analysis. Variance inflation factor (VIF) and tolerance diagnostics were checked to assess multicollinearity. The sample size was determined with a minimum of 10 participants needed per predictor variable. With 12 potential predictors to be tested, the sample size was set at 120 participants.[23] The pairwise deletion was used with regard to the missing values.

All statistical analyses were performed using IBM SPSS V.22.0.0.1.

RESULTS

Between December 2014 and July 2017, 370 eligible patients were identified. A total of 157 were excluded as baseline health outcomes were missing, 36 refused participation, 19 did not return the follow-up questionnaires, 14 were insufficient proficient in Dutch, 13 died, 6 were excluded due to behavioural disorders, and 5 were not reachable by phone. The patient characteristics of both the study population and excluded patients are summarised in table 1. There were no statistically significant differences between the study population and the excluded patients. With the use of pairwise deletion for missing values, the variables HADS depression score, MCS and PCS had one participant with missing data, HADS anxiety score had two participants with missing data and mRS baseline score had 38 participants with missing data. The average number of days between the stroke date and the follow-up date was slightly higher than planned, (*M*=379.3 days, SD=47.1).

The mRS was slightly higher after 1 year without reaching statistical significance as compared with baseline. The SSADQ score however, was statistically significantly better after 1 year. The RAND-36 subscales 'role limitations due to physical problems', 'role limitations due to mental problems', and 'health change' were statistically significantly higher than baseline scores, reaching the range of 3–5 points for a minimally clinically important difference (tables 2 and 3 and figure 2).

Predictors of QoL

Mental component

For the mental component of the RAND-36, we found two predictors that explained 39.8% of the variance, with R^2=0.398, R^2 adjusted=0.387 and F=37.638 (2, 114) (p<0.001). The results are summarised in table 4.

Physical component

For the physical component of the RAND-36, we found three predictors explaining 26.1% of the variance, with R^2=0.261, R^2 adjusted=0.241 and F=13.392 (3, 114) (p<0.001). The results are summarised in table 4.

DISCUSSION

In this study, we found that depression and anxiety at baseline predicted a worse mental component of QoL after 1 year as measured with the RAND-36 in patients discharged home after a TIA or minor stroke. Depression at baseline, but also age and being a woman, predicted a worse physical component of QoL after 1 year. These findings might be important for selecting patients for interventions to prevent unforeseen problems long after their TIA or minor stroke.

In these patients, we also found a slight improvement of QoL after 1 year as measured with the RAND-36, without being clinically significant. Van Mierlo *et al* also reported modest improvements in QoL in a population with more severe stroke patients, but mostly in the first 6 months after onset and more pronounced in activities of daily life(ADL)-independent patients.[24] Our study confirms that in ADL-independent patients after stroke, the QoL also improves within 1 year, but less obvious than in the previous study. We think that this is a reflection of coping

Table 1 Comparison of patient characteristics of the study population and the excluded patients

Characteristic	N=120	Excluded patients (N=250)	P value
Age, y, mean (SD)	68.6 (11.5)	68.4 (12.1)	0.891*
Sex			0.155†
Female	43 (35.8)	109 (43.6)	
Male	77 (64.2)	141 (56.4)	
Diagnosis			0.360†
TIA	29 (24.2)	50 (20.0)	
Minor stroke	91 (75.8)	200 (80.0)	
Localisation			0.508‡
Right hemisphere	31 (25.8)	75 (30.0)	
Left hemisphere	55 (45.8)	101 (40.4)	
Vertebrobasilar	30 (25.0)	56 (22.4)	
Ocular	0 (0.0)	3 (1.2)	
Other	4 (3.3)	15 (6.0)	
Stroke incidence			0.267†
Relapse	20 (16.7)	54 (21.6)	
First ever	100 (83.3)	196 (78.4)	
Marital status		n/a	
Married	61 (50.8)		
Unmarried	44 (36.7)		
Widowed	15 (12.5)		
Education		n/a	
Low	12 (10.0)		
Average	58 (48.3)		
High	49 (40.8)		
Living arrangement		n/a	
Alone	51 (42.5)		
With spouse/relative(s)	68 (56.7)		

All data are expressed as n (%), except where specified.
* *t*-test
† χ^2 test
‡ Fisher exact test
TIA, transient ischaemic attack.

mechanisms in the chronic phase when patients still have handicaps of problems after their stroke or TIA.

In this study, we found four predictors for a lower QoL after 1 year, but depression was the only one that was significant in both domains of QoL. The more symptoms of depression, as measured with the HADS at baseline, the worse the mental and physical component of QoL was after 1 year. Depression at baseline is frequently seen in patients who suffered from a stroke.[25] A review estimated that one third of stroke survivors suffered from depression at any time up to 5 years after stroke.[26] The finding that depression at baseline is a predictor for worse QoL after a TIA or minor stroke was well in line with a previous study, that showed that poststroke depression in the acute phase after stroke predicts worse QoL, 1 year after TIA or minor stroke.[27] Another study found that poststroke depression

Table 2 SSADQ and MRS scores at baseline and follow-up (paired samples *t*-test)

	Baseline		Follow-up				
	Mean (SD)	N	Mean (SD)	N	95% CI	*t*-value (df)	P value
SSADQ score	17.1 (8.3)	90	13.5 (8.3)	90	2.119 to 5.037	4.87 (89)	<0.001
mRS score	1.0 (0.8)	77	1.2 (0.9)	77	−0.372 to 0.009	−1.90 (76)	0.061

SSADQ, Stroke-Specific Anxiety Depression Questionnaire; mRS, modified Rankin Scale.

Table 3 HADS and RAND-36 scores at baseline and follow-up (Wilcoxon signed-rank test)

	Baseline		Follow-up			
	Mean (SD)	N	Mean (SD)	N	Z-score	P value
HADS depression	4.3 (4.1)	119	4.2 (4.1)	119	−0.759	0.448
HADS anxiety	4.6 (3.6)	118	4.3 (3.8)	119	−1.089	0.276
RAND-36 physical component	44.8 (10.2)	116	45.0 (11.4)	119	−1.225	0.221
RAND-36 mental component	46.1 (11.1)	116	47.7 (11.1)	119	−1.451	0.147

HADS, Hospital Anxiety Depression Scale; RAND-36, Reseach and Development-36 scale.

has a high association with disability and poor QoL 1 year after minor stroke.[28] We think that early depressive symptoms might be a criterion in our patients to select the ones who need aftercare soon after their TIA or minor stroke.

The anxiety scale of the HADS was found to be a predictor for a worse mental component and not for a worse physical component of the RAND-36. Previous research also found that poststroke anxiety is less important than poststroke depression as a predictor for QoL.[29] Nevertheless, an association was found in several studies between poststroke anxiety and QoL[29–32] and anxiety early after TIA or minor stroke might also be a reason to offer more active stroke aftercare.

In our study, women have a lower physical QoL after stroke, in comparison with men. This result is in line with previous studies that found that women have worse HRQoL after stroke, in comparison with men.[33 34] A higher prevalence of disability and a greater age at stroke onset in women could be a possible explanation for this finding.[35] It is important to realise that in previous research in the general population, women had worse HRQoL compared with men even without having a disease.[36] However, socioeconomic status and sociodemographic characteristics such as race and education might be an explanation for the differences in that study. Age itself was found to be a predictor for physical QoL. This is also in line with another study that stated that as the population ages, the number of strokes and therefore stroke survivors with poor QoL increases.[37]

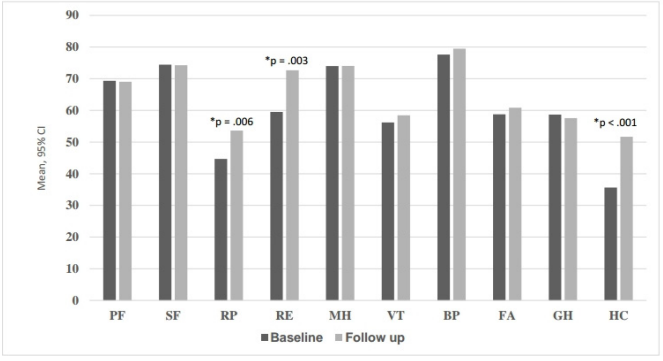

Figure 2 Bar graph of RAND-36 subscale scores at baseline and follow-up. BP, bodily pain; FA, fatigue; GH, general health; HC, health change; MH, mental health; PF, physical functioning; RE, role limitations due to mental problems; RP, role limitations due to physical problems; SF, social functioning; VT, vitality. *Statistically significant difference.

Table 4 Predictors of QoL after 1 year (multiple linear regression analysis)

	B	SE	β	*t*-value	P value
Mental component					
Constant	56.14	1.32		42.52	<0.001
HADS depression	−1.35	0.25	−0.5	−5.47	<0.001
HADS anxiety	−0.57	0.28	−0.19	−2.07	0.041
Physical component					
Constant	65.13	6.1		10.67	<0.001
Age	−0.26	0.08	−0.27	−3.25	0.002
Sex	4.1	1.92	0.18	2.14	0.034
HADS depression	−1.1	0.23	−0.4	−4.9	<0.001

HADS, Hospital Anxiety Depression Scale; QoL, quality of life.

The strength of our study is the prospective nature of our cohort in which possible predictors have been included that have been carefully selected based on previous research. A limitation of this study is the fact that a substantial part of our study population of patients who suffered a TIA or minor stroke was excluded due to several reasons. However, there were no differences in patient characteristics between the study population and the excluded patients. Another limitation is that during the year between baseline and follow-up, there was no insight into outpatient rehabilitation care, changes in medication or employment.

Conclusions

In this study, we found that baseline depression and anxiety predicted worse mental QoL, whereas baseline depression, age and sex predicted worse physical QoL. With the identification of these predictors, we might be able to select more efficiently and timely the patients with TIA or minor stroke who need stroke aftercare.

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Contributors VIHK: designed the work and had substantial contributions to the acquisition, analysis, and interpretation of data, in drafting the work and revising it critically for important intellectual content, and gave final approval of the version to

be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. EB: gave substantial contributions to the acquisition, analysis, and interpretation of data, in drafting the work and revising it critically for important intellectual content, and gave final approval of the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. K-HL: gave substantial contributions to the acquisition, analysis, and interpretation of data, in drafting the work and revising it critically for important intellectual content, and gave final approval of the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. EB and K-HL: contributed equally to this work. All authors have confidence in the integrity of each other's contributions.

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